EXHIBIT B

Report re Gynecare TVT-Obturator

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This report contains my opinions regarding the TVT-Obturator ("TVT-O") device, which are based on my education, training, experience, as well as my review of published medical literature and other materials cited in this report and referenced on the attached list of materials. I hold all opinions set forth in this report to a reasonable degree of medical certainty, and I reserve the right to supplement or amend my opinions if I receive additional information after I sign the report.

I have not testified as an expert at trial or by deposition in the previous four years. I am being compensated $400 per hour for my time spent working on this matter.

I. Background

a. Education and Training

I attended Stanford University for my undergraduate work, where I completed a dual degree, receiving a B.S. degree in Biological Sciences and an A.B. in classical studies. I then attended medical school at the University of California San Diego, graduating in 1992. I did my internship and residency at the hospitals at the University of Pennsylvania, where I received the UPenn School of Medicine student teaching award in 1994 and completed my residency in 1996. I am presently employed at Pacific Central Coast Clinics as an OB-GYN physician, with a special interest in pelvic floor surgery. I am board certified in obstetrics and gynecology.

I am a member of the American College of Obstetricians and Gynecologists, the American Urogynecologic Society, and the American Medical Association. I have served as a preceptor for American Medical Systems for their Elevate and Mini-Arc vaginal mesh products.

A copy of my curriculum vitae is being provided with this report.

II. Stress Urinary Incontinence

a. Definition, Prevalence, Risk Factors

Stress urinary incontinence (SUI) is an unintentional loss of urine that occurs when physical activity such as coughing, sneezing, running, laughing, or lifting puts pressure on the bladder. It is a common condition that affects at least 15-80% of women.[1] SUI also affects women at an increasing rate

[1] Schimpf MO, et al., Sling surgery for stress urinary incontinence in women: a systematic review and metaanalysis. Am J Obstet Gynecol 2014;210:1.e1-1.e27.

as they age.[2] Risk factors for SUI include childbirth, pregnancy, age, menopause, smoking, obesity, constipation, lifting, race, and pelvic organ prolapse.[3]

b. Impact on Quality of Life and Economic Impact

SUI can significantly affect quality of life. It can interfere with activities, social interactions, and sexual relationships, and can cause women to wear incontinence diapers.[4] SUI can lead to urinary tract infections and depression. It can cause embarrassment and anxiety, and interference with social activities. Patients very commonly report these things to me in my practice both spontaneously and after direct questioning. Unfortunately, the literature suggests that less than half of women who have incontinence report it to their health care providers.[5] 63% of women with SUI also have associated prolapse.[6]

The economic impact of urinary incontinence is significant. It has been estimated that the direct cost of urinary incontinence care in the United States is $19.5 billion.[7]

III. Treatment Options for SUI

Treatment options for SUI include:

a. Non-Surgical SUI Treatment Options

Pelvic floor muscle training such as Kegel exercises, biofeedback, and vaginal weights are non-surgical means of treating SUI. Incontinence in 15-28% of women is 100% cured by pelvic floor muscle training (PFMT). 25-50% of women primarily treated with PFMT to try to improve or cure their incontinence will undergo surgery.[8] Pelvic floor muscle training works for some but not all patients.

Pessaries are another non-surgical treatment option. I offer them to patients, but women often do not accept them due to vaginal discharge, discomfort, and embarrassment relating to the idea of wearing a pessary. They are "best used for women who are poor surgical candidates or who choose not to have surgery."[9] There are no drugs that are FDA approved to treat SUI.[10]

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[2] Nygaard I, et al., Prevalence of symptomatic pelvic floor disorders in US women. JAMA 2008 Sep 17; 300 (11): 1311-16.
[3] Wood LN and Anger JT, Urinary incontinence in women, BMJ:2014;349:g4531.
[4] Fultz, NH, et al., Burden of stress urinary incontinence for community-dwelling women. (Am J Obstet Gynecol 2003 Nov; 189(5): 1275-1282.
[5] Wu JM, et al., Prevalence and incidence of urinary incontinence in a diverse population of women with noncancerous gynecologic conditions. Female Pelvic Med Reconstr Surg 2010; 16(5): 284-28; ACOG/AUGS Practice Bulletin No. 155; Nov. 2015.
[6] Gallentine ML and Cespedes RD, Occult stress urinary incontinence and the effect of vaginal vault prolapse on abdominal leak point pressures. Urology 2001 Jan; 57(1):40-44.
[7] ACOG/AUGS Practice Bulletin No. 155; Nov. 2015.
[8] Labrie J, et al., Protocol for Physiotherapy OR Tvt Randomised Efficacy Trial (PORTET): a multicenter randomised controlled trial to assess the cost-effectiveness of the tension free vaginal tape versus pelvic floor muscle training in women with symptomatic moderate to severe stress urinary incontinence. BMC Women's Health 2009; 9:24.
[9] Wood LN and Anger JT, Urinary incontinence in women, BMJ:2014;349:g4531.
[10] Wood LN and Anger JT, Urinary incontinence in women, BMJ:2014;349:g4531.

b. Surgical SUI Treatment Options

All SUI surgeries have shared risks such as hematoma, bladder or bowel injury, lower urinary tract infection, vascular injury, infection, urinary retention, persistent SUI, bleeding, pain, dyspareunia, fistula, de novo urge incontinence, and worsening urge incontinence.[11] There are numerous SUI surgeries, including the following:

i. Native/Tissue Tension Repairs

Surgical native tissue and tension repairs include the Kelly plication, Pereyra needle urethropexy, and abdominal operations such as the Burch colposuspension and Marshall-Marchetti-Krantz ("MMK") cystourethropexy.

The MMK procedure is a bladder neck suspension surgery. After the patient is placed under general anesthesia, an incision is made in the lower abdomen, sutures are placed in the tissues near the bladder neck and urethra, and are attached to the pubic bone or tissue behind the pubic bone, thereby supporting the bladder neck. This surgery requires several days of hospitalization. It is no longer a favored technique because of its risks, postop morbidity, and slightly inferior long-term efficacy. Transvaginal needle suspension procedures likewise are rarely performed today, primarily because they have been shown to be significantly less effective than Burch and sling procedures.

The Burch procedure was introduced in 1961 and is a variation of the MMK procedure. It involves the use of sutures placed just lateral to the bladder neck and attached to Cooper's ligament. It generally requires a three-day hospitalization if performed as an open procedure. One long-term study of the efficacy of the Burch procedure found that only 19% of patients undergoing the Burch procedure reported no incontinence episodes at 14 years (median) follow-up.[12] The study further found that lower urinary tract symptoms are very common at long-term follow-up after the Burch procedure, with more than three-fourths of the patients experiencing such symptoms. Other literature reports that the Burch procedure is an effective incontinence procedure, but it has increased morbidity over other techniques such as mesh midurethral slings, discussed below. There is also an increased incidence of other pelvic organ prolapse—particularly enterocele—following the Burch procedure.

The pubovaginal sling procedure uses the patient's own tissue—either rectus fascia or fascia lata—to support the bladder neck. The procedure requires multiple incisions, as the patient's fascia must be harvested from the patient before it can be used. The Stress Incontinence Surgical Treatment Efficacy Trial ("SISTEr"), a randomized clinical trial comparing 655 women who underwent either the Burch procedure or pubovaginal sling procedure using autologous rectus fascia reported that after seven years' follow-up, only 27% of women undergoing a pubovaginal sling procedure were continent, down from 52% at two years after the procedure. Only 13% of the patients who received treatment with the Burch procedure were continent after seven years, down from 42% at two years.[13]

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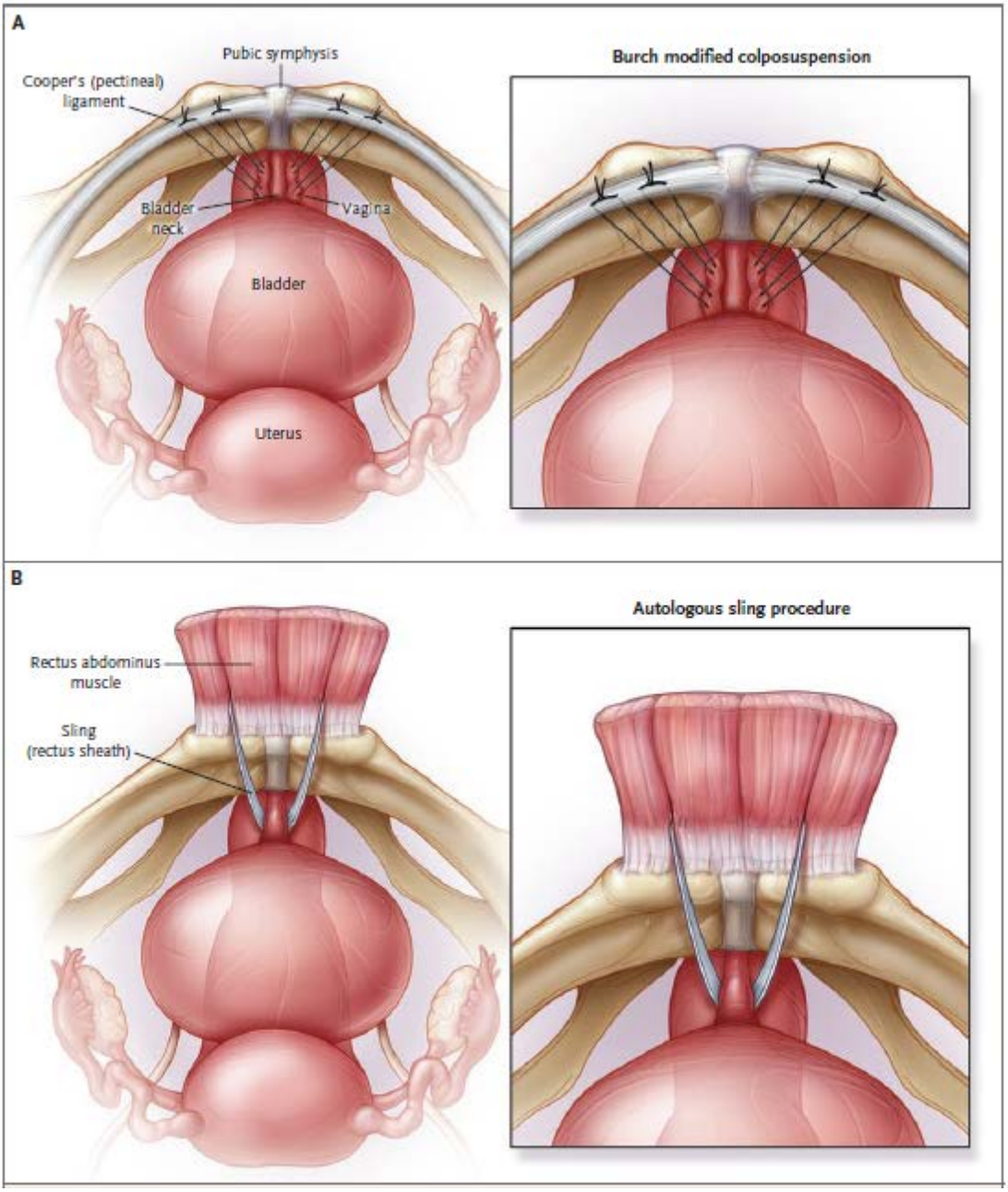
[11] ACOG/AUGS Practice Bulletin No. 155; Nov. 2015.
[12] Kjolhede P, Long-term efficacy of Burch colposuspension: a 14-year follow-up study. Acta Obstet Gynecol Scand 2005:84:767–72.
[13] Richter HE, et al., Patient Related Factors Associated with Long-Term Urinary Continence After Burch Colposuspension and Pubovaginal Fascial Sling Surgeries. Urology 2012 Aug;188:485-89.



Illustrations from Albo ME, et al., Burch Colposuspension versus Fascial Sling to Reduce Urinary Stress Incontinence. N Engl J Med 2007;356:2143–55.

ii. Other Treatment Options

Urethral bulking agents are another treatment option for SUI. They can be effective in treating SUI, but are not long-lasting, leading many patients to pursue other surgical options. These are often offered to patients who are poor surgical candidates or who have failed other surgical treatment options.

IV. Clinical Experience & Personal Experience with SUI Treatments

During my residency, I was trained in treatments for SUI, including Burch colpourethropexy and needle procedures such as the Raz and Pereyra techniques. My principal experience was in what was then considered the "gold standard"—the Burch procedure.

The TVT was introduced in the late '90s, hence I did not receive training in residency on the use of mid-urethral slings. I learned the procedures after residency, due to the ever-growing body of literature which supported their efficacy in the setting of marked improvement in return to normal function.

I performed Burch colpourethropexies almost exclusively for the treatment of female stress urinary incontinence until 2002. The demographics in my community (elderly, Caucasian predominantly) resulted in my seeing a large number of women with incontinence. I was satisfied, and remain satisfied with this procedure, but almost never perform it anymore due to the profound difference in recovery time required for the patient. The Burch is a technically challenging procedure, with vastly increased complications and efficacy, particularly in obese patients. The risk of bladder perforation is vastly greater (in fact, during my training I was taught to iatrogenically injure the bladder on every case in order to confirm correct suture placement) than with the TVT-O device. The risk of postop urinary retention is also far greater, and my standard practice with the Burch is to maintain a Foley catheter for 3 days postop, and counsel patients that at times 1-2 weeks of catheterization is likely. As my interest and expertise in pelvic floor repairs increased over time, I also became concerned about the changes in dynamics of pressure on the pelvic floor that occur with Burch. My incontinence surgeries have been successful in general, but over the years many of my Burch patients developed enteroceles that needed subsequent repair, a problem that is unlikely to occur with TVT-O.

In the hope that my patients would experience less postop pain and have a quicker return to normal activities, in the past I would also work closely with the local urologists in my community and would have them perform fascial and xenograft sling procedures concomitantly with my pelvic floor repairs, when indicated. However, even in these cases, I was often impressed by the large amount of blood loss involved, and also with the postop voiding dysfunction and pain related to the fascial sling.

When the TVT was first introduced, I waited until there was a wealth of peer-reviewed data surrounding it before adopting it into my practice, but I have been overwhelmingly pleased with the results since I have adopted it and other mid-urethral slings. I routinely have patients approach me at the grocery store and at social events with tears of gratitude in their eyes for the improvement they have experienced in their quality of life from the mesh sling procedure. While I still counsel my patients that they must be prepared for immediate and delayed postop complications, and I recommend at least two weeks off work, for the most part those patients I have had that only required a sling, without other pelvic floor work, have been working at their normal daily activities and jobs within 3 days. This would have been simply unheard of following a Burch procedure.

V. Ethicon's TVT-O Mid-Urethral Slings

a. Historical Use of Polypropylene

Polypropylene has been used successfully and safely for many years. It has been used for hernia repairs for over thirty years and for open abdominal sacrocolpopexies for almost fifty years. Prolene sutures are made of polypropylene, and have been extensively used. They are the sutures typically used in the Burch procedure.

b. Development of Tension-Free Vaginal Tape (TVT) Using Prolene Mesh

Surgeons have been using synthetic mesh to treat SUI since the 1960s.[14] Mid-urethral tension-free slings, however, were first developed by Dr. Ulf Ulmsten in collaboration with Dr. Peter Petros. Drs. Ulmsten and Petros evaluated several possible materials and ultimately selected Prolene mesh, finding it to be "the ideal material."[15] During the development process, they used different materials such as Teflon, Mersilene, Gore-Tex, and Marlex, but those materials were not used because each of them caused a significant amount of tape rejection.[16] They noted that they found that "Mersilene was easy to use, non-stretch, and effective, but it had a high erosion rate (14%)."[17] They selected polypropylene mesh tape because by 1996, it "had solved the problem of erosions and become universally accepted." They found that women implanted with Prolene mesh did not experience tape rejection, and the Prolene tape induced a minimal inflammatory reaction.[18] The sling was created after the discovery that "a hemostat applied immediately behind the pubic symphysis at the level of the midurethra controlled urine loss on coughing" and it was based on what was dubbed "the integral theory."[19] The integral theory posited that "loose ligaments caused both stress and urge incontinence, albeit for different reasons: inactivation of urethral closure forces for USI and activation of the micturition reflex prematurely for urge incontinence." Ethicon became interested in the product after Dr. Axel Arnaud visited Dr. Ulmsten in Sweden in 1995, observed Dr. Ulmsten perform the TVT procedure, and realized that the procedure "had the potential to replace the current gold standard namely the Burch procedure which required general anesthesia, was not easy to perform particularly endoscopically and moreover had quite poor long term results."[20] The TVT was introduced in the U.S. in 1998, and soon became the gold standard for SUI surgical treatment.

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[14] Welk B, et al., Removal or Revision of Vaginal Mesh Used for the Treatment of Stress Urinary Incontinence. JAMA Surg. 2015 Dec;150(12):1167-75.

[15] Petros PE, Creating a gold standard surgical device: scientific discoveries leading to TVT and beyond: Ulf Ulmsten Memorial Lecture 2014. Int Urogynecol J 2015 Apr; 26(4):471-6; Ulmsten U et al, A multicenter study of tension-free vaginal tape (TVT) for surgical treatment of stress urinary incontinence. Int Urogynecol J Pelvic Floor Dysfunct 1998;9(4):210-213; Petros, PE, Ulmsten UI, An integral theory and its method for the diagnosis and management of female urinary incontinence. Scand J Urol Nephrol Suppl 1993; 153:1-93.

[16] Falconer C, et al., Influence of Different Sling Materials on Connective Tissue Metabolism in Stress Urinary Incontinent Women. Int Urogynecol J 2001 (Suppl 2):S19-S23.

[17] Petros PE, Creating a gold standard surgical device: scientific discoveries leading to TVT and beyond: Ulf Ulmsten Memorial Lecture 2014. Int Urogynecol J 2015 Apr; 26(4):471-6.

[18] Falconer C, et al., Influence of Different Sling Materials on Connective Tissue Metabolism in Stress Urinary Incontinent Women. Int Urogynecol J 2001 (Suppl 2):S19-S23.

[19] Petros PE, Creating a gold standard surgical device: scientific discoveries leading to TVT and beyond: Ulf Ulmsten Memorial Lecture 2014. Int Urogynecol J 2015 Apr; 26(4):471-6.

[20] Arnaud A, The History of TVT, 2000 Jul 12.

The TVT is a monofilament, large-pore (Type I),[21] lightweight, Prolene polypropylene mesh sling that is placed without tension under the mid-urethra. The mesh is 1.1 cm x 45 cm, and is covered by a plastic sheath. It is attached to two stainless steel needles used to implant the device. The pore size is approximately 1,300 microns, and the weight is approximately 100 g/m^2.[22] The sling courses from the mid-urethra up behind the pubic bone, exiting via two small suprapubic incisions. The TVT supports the urethra during sudden movements such as a cough or sneeze to allow the urethra to remain closed so that the leakage of urine is prevented. The procedure itself is a minimally invasive, quick procedure whose efficacy can be tested immediately. Cystoscopy is performed to ensure that the bladder has not been perforated by the procedure.

The TVT is the most extensively studied mid-urethral sling, having been the subject of more than 100 randomized controlled trials. Studies have shown polypropylene mesh mid-urethral slings like the TVT to have high efficacy and low complication rates.[23] The TVT was found to have a similar cure rate to open Burch procedures, with less recovery time and less cost.[24] Many long-term studies involving the TVT sling demonstrate its safety and efficacy.[25]

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[21] Amid PK, Classification of biomaterials and their related complications in abdominal wall hernia surgery. Hernia 1997;1:15-21.

[22] Moalli PA, et al., Tensile properties of five commonly used mid-urethral slings relative to the TVT. Int Urogynecol J 2008;19:655–63.

[23] Ford AA, Rogerson L, Cody JD, Ogah J. Mid-urethral sling operations for stress urinary incontinence in women. Cochrane Database of Systematic Reviews 2015, Issue &. Art. No.: CD006375. DOI:10.1002/14651858.CD006375.pub3; Cox, A, Herschorn S. Lee L, Surgical management of female SUI: is there a gold standard? Nature 2013; 10:78-89; Schimpf MO, et al., Sling surgery for stress urinary incontinence in women: a systematic review and metaanalysis. Am J Obstet Gynecol 2014;210:1.e1-1.e27; Tommaselli GA, et al., Medium-term and long-term outcomes following placement of midurethral slings for stress urinary incontinence: a systematic review and metaanalysis. Int Urogynecol J 2015; Ogah, J., Cody, JD, Rogerson, L, Minimally invasive synthetic suburethral sling operations for stress urinary incontinence in women. Cochrane Database of Systematic Reviews 2009, Issue 4. Art. No.: CD006375. DOI:10.1002/14651858.CD006375.pub2; Nilsson CG, et al., Seventeen years follow-up of the tension-free vaginal tape procedure for female stress urinary incontinence. Int Urogynecol J 2013 Aug; 24(8):1265-9.

[24] Nilsson CG, et al., Seventeen years follow-up of the tension-free vaginal tape procedure for female stress urinary incontinence. Int Urogynecol J 2013 Aug; 24(8):1265-9.

[25] Laurikainen E, et al., Five-year Results of a Randomized Trial Comparing Retropubic and Transobturator Midurethral Slings for Stress Incontinence. Eur Urol 2014 Jun;65(6):1109–14; Kuuva N, et al., Long-term results of the tension-free vaginal tape operation in an unselected group of 129 stress incontinent women. Acta Obstet Gynecol 2006;85(4):482-487; Heinonen P, et al., Tension-free vaginal tape procedure without preoperative urodynamic examination: long-term outcome. Int J Urol. 2012 Nov;19(11):1003-9; Aigmueller T, et al., Ten-year follow-up after the tension-free vaginal tape procedure. Am J Obstet Gynecol 2011 Nov;205(5):496.e1-5; Olsson I, et al., Long-term efficacy of the tension-free vaginal tape procedure for the treatment of urinary incontinence: a retrospective follow-up 11.5 years post-operatively. Int Urogynecol J 2010 Jun;21(6):679–683; Liapis A, et al., Long-term efficacy of tension-free vaginal tape in the management of stress urinary incontinence in women: efficacy at 5- and 7-year follow-up. Int Urogynecol J 2008 Nov;19(11):1509-1512; Serati M, et al., TVT for the Treatment of Urodynamic Stress Incontinence: Efficacy and Adverse Effects at 13-Year Follow-Up. Neurourol and Urodynamics DOI 10.1002/nau; Svenningsen R, et al., Long-term follow-up of the retropubic tension-free vaginal tape procedure. Int Urogynecol J. 2013 Aug;24(8):1271-8; Prien-Larsen JC, et al., Long-term outcomes of TVT and IVS operations for treatment of female stress urinary incontinence: monofilament vs. multifilament polypropylene tape. Int Urogynecol J 2009 Jun;20(6):703-709; Chêne G, et al., Long-term results of tension-free vaginal tape (TVT) for the treatment of female urinary stress incontinence. Eur J Obstet Gynecol Reprod Biol 2007 Sep;134(1):87-94; Vesna Bjelic-Radisic V, Patient-related Outcomes and Urinary Continence Five Years After the Tension-Free Vaginal Tape Operation, Neurourology and Urodynamics 2011;30(8):1512-1517; Jin-Yan Wu JY, et al., Surgical therapies

c. Development of the TVT-Obturator

Following the success of the TVT sling, Ethicon developed the TVT-Obturator ("TVT-O") device. The TVT-O is very similar to the TVT (and utilizes the same Prolene mesh described above), but has a hammock-type support rather than u-type support under the mid-urethra, has less risk of bladder perforation. The TVT-O was based on a modification of the TVT procedure developed by a French surgeon, Dr. Delorme.[26] Ethicon developed the sling in collaboration with Dr. de Leval, a Belgian Professor of Urology.

The TVT-O consists of a 1.1 x 45 cm strip of blue Prolene polypropylene Type I mesh attached to two stainless steel curved helical passers that are used to implant the device. It also comes with a stainless steel Atraumatic Winged Guide that facilitates passage of the helical passers through the dissection tract. It "is intended to be used in women as a sub-urethral sling for the treatment of stress urinary incontinence (SUI) resulting from urethral hypermobility and/or intrinsic sphincter deficiency."[27]

The TVT-O traverses through the obturator membrane and exits the medial thighs rather than the abdomen. It has a short learning curve, low morbidity, a short operating time, and is simple to perform, which makes it available to more women.[28] It was first introduced in the U.S. in 2004. As discussed below, there are numerous medium- and long-term studies of the TVT-O that support the safety and efficacy of the device.

d. The Safety and Utility of the TVT-Obturator

Liapis and colleagues reported on 111 patients who were treated with a TVT-O device either with or without a concomitant anterior colporrhaphy, and found an objective cure rate in the TVT-O only patients of 82.4%, with improvement in an additional 6.8%. They found an objective cure rate of 80.5% in the group of patients who underwent both TVT-O and anterior colporrhaphy, with improvement in an additional 7.4% of those patients.[29]

Angioli and colleagues published the results of their prospective five-year randomized controlled trial comparing seventy-two patients with SUI treated with either TVT or TVT-O. They found that 72.9% of the TVT-O patients had their SUI cured, and complication rates were low after five years. The authors concluded that both techniques were safe, and noted that dyspareunia occurred in only 3.3% of patients. Eighty-five percent of the patients reported that they would undergo the same procedure again if SUI

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of female stress urinary incontinence: experience in 228 cases, Int Urogynecol J 2010 Jun;21(6):645-649; Song PH, et al., The 7-year outcome of the tension-free vaginal tape procedure for treating female stress urinary incontinence. BJU Int 2009 Oct;104(8):1113-1117; Celebi I, et al., Results of the tension-free vaginal tape procedure for treatment of female stress urinary incontinence: a 5 year follow-up. Arch Gynecol Obstet 2009 Apr;279(4):463-467; Jelovsek JE, et al, Randomized trial of laparoscopic Burch colposuspension versus tension-free vaginal tape: long-term follow up. BJOG 2008 Jan;115(2):219-225; McCracken GR, et al., Five Year Follow-up Comparing Tension-Free Vaginal Tape and Colposuspension, Ulster Med J 2007 Sep;76(3):146-149.

[26] Arnaud A, The History of TVT-O, 2007 Jan 16.

[27] ETH.MESH.02340974-80; ETH.MESH.00860239-45.

[28] Groutz A, et al., Long-Term Outcome of Transobturator Tension-Free Vaginal Tape: Efficacy and Risk Factors for Surgical Failure. J Women's Health 2010;20(10):1525-1528.

[29] Liapis A, et al., Efficacy of inside-out transobturator vaginal tape (TVTO) at 4 years follow up. Eur J Obstet Gynecol Reprod Biol 2010;148:199–201.

recurred, especially within the TVT-O group. Only one of the three erosions that occurred were symptomatic.[30]

In 2011, Dr. Asnat Groutz and colleagues reported on the five-year results of their prospective study of sixty-five patients who underwent a TVT-O procedure for treatment of SUI. Seventy-four percent of the sixty-one patients available for follow-up had their SUI cured, and an additional 8% had their SUI improved. Only two patients experienced vaginal erosion, neither of which were cases of late tape erosion. The most common complication reported was residual pain, but that occurred in only 2.7% of patients. The authors noted that the TVT-O procedure "is technically simple and, therefore, is associated with a short learning curve, short operating time, and low morbidity."[31]

Drs. Dali Cheng and Caigang Liu reported the results of their prospective trial of TVT-O patients with five-year follow-up in the European Journal of Obstetrics & Gynecology and Reproductive Biology in 2012. They studied 103 patients with SUI, and observed a complete disappearance of SUI in 87.4% of patients. Ninety-two percent of the patients were improved. They also found that the cure rates remained constant between years one and five after the procedure. In 90 of the 103 patients studied, their frequency and urge symptoms were significantly improved at five-year follow-up. Incontinence severity and quality of life scores were largely improved after the procedure, and again remained constant from years 1 to 5. The authors observed only one case of tape erosion, one wound infection, and no cases of bladder injury, vascular injury, or neurologic injury. Groin pain was found in twenty-five patients in the first six months, but that rate was done to 3.8% by the one-year mark. They concluded that the study's findings suggested that the TVT-O was a safe and effective procedure for treatment of patients with SUI.[32]

Serati and colleagues published the five-year results of a multi-center prospective observational study of TVT-O patients in 2013. They studied 191 women with pure SUI who were treated with the TVT-O and found that at five-year follow-up, the subjective and objective cure rates were 90.3% and 90.8%, respectively. De novo overactive bladder occurred in 24.3% of the patients at one year and by 19.5% at five-year follow-up. Only one patient (0.5%) experienced a bladder perforation, and there were no other intra-operative complications observed. Early post-operative voiding dysfunction occurred in eleven women, but only one of those required revision surgery. Vaginal erosion was observed at one year after the procedure in two cases. Groin pain was reported by 9.9% of the patients in the first day after surgery, but by one month after surgery, the rate was down to only 3.1%. By one year, it further dropped to 1%; occurring in only two women.[33]

Laurikainen and colleagues reported on the five-year results of their multi-center randomized clinical trial comparing TVT and TVT-O for SUI in 2014. They studied 268 women who underwent either TVT or TVT-O to treat their incontinence, and saw an objective cure rate of 84.7% in the TVT group and 86.2% in the TVT-O group. 91.7% of the TVT-O patients and 94.2% of the TVT patients were

[30] Angioli R, et al., Tension-Free Vaginal Tape Versus Transobturator Suburethral Tape: Five-Year Follow-up Results of a Prospective Randomised Trial. Eur Urol 2010;58:671–77.
[31] Groutz A, et al., Long-Term Outcome of Transobturator Tension-Free Vaginal Tape: Efficacy and Risk Factors for Surgical Failure. J Women's Health 2011;20(10): 1525–28.
[32] Cheng D and Liu C, Tension-free vaginal tape-obturator in the treatment of stress urinary incontinence: a prospective study with five-year follow-up. Eur J Obstet Gynecol Reprod Biol 2012;161:228–31.
[33] Serati M, et al., TVT-O for the Treatment of Pure Urodynamic Stress Incontinence: Efficacy, Adverse Effects, and Prognostic Factors at 5-Year Follow-up. Eur Urol 2013;63:872–78.

subjectively satisfied with their treatment. The authors saw no late-onset adverse effects of the tape material, and they saw only one erosion at one year post-operatively. Both cohorts showed a significant improvement from pre-operative scores in all condition-specific quality of life questionnaires. De novo overactive bladder occurred in only 2.4% of the TVT-O patients and 3.1% of the TVT patients, but 84% of the women who had urgency symptoms pre-operatively were cured of their urgency symptoms by the procedures.[34]

Dr. Stavros Athanasiou and colleagues published seven-year data from their retrospective study of 124 consecutive women who had their SUI treated with a TVT-O device. The objective cure rate was 81.5%, and the subjective cure rate was 83.5%. De novo urgency was experienced by 7% of the patients, and only one patient (0.8%) had post-operative voiding difficulties that required tape division three months post-operatively. Only one vaginal erosion was observed (0.8%)—a midline erosion diagnosed at one year. No erosions were detected at the follow-up visit. No patient reported persistent groin pain at follow-up.[35]

Because of their excellent efficacy and safety data as reflected in the studies discussed in this report, full-length polypropylene mesh midurethral slings like the TVT and TVT-O are considered the gold standard for the surgical treatment of stress urinary incontinence.[36]

The design of the TVT-O is state of the art. The TVT device, which utilizes the same mesh as the TVT-O, has been the subject of more than 100 RCTs and many long-term studies. The TVT-O also is extensively studied. The TVT-O has macroporous (greater than 75 microns) monofilament polypropylene mesh. Polypropylene has been the most popular material used in incontinence slings, and is used in the slings of many different companies. It has "emerged as the standard of care because of lower reported rates of erosion/extrusions (0%-5%) compared with other forms of synthetic slings."[37] The TVT-O mesh has a large pore size (1.1 cm) for a small strip of mesh, which promotes mechanical anchorage with collagen and allows macrophages and fibroblasts to enter the pores. "A pore size in excess of 75 µm facilitates the migration of macrophages and leukocytes. This property is intended to reduce the infective risk, which predisposes to extrusion or erosion of the prosthetic material."[38]

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[34] Laurikainen E, et al., Five-year Results of a Randomized Trial Comparing Retropubic and Transobturator Midurethral Slings for Stress Incontinence. Eur Urol 2014 Jun;65(6):1109-14.

[35] Athanasiou S, et al., Seven years of objective and subjective outcomes of transobturator (TVT-O) vaginal tape: Why do tapes fail? Int Urogynecol J. 2014;25:219–25.

[36] Cox A, et al., Surgical management of female SUI: is there a gold standard? Nat Rev Urol 2013 Feb;10:78–89; Nilsson CG, et al., Seventeen years follow-up of the tension-free vaginal tape procedure for female stress urinary incontinence. Int Urogynecol J 2013 Aug; 24(8):1265-9; Heinonen P, et al., Tension-free vaginal tape procedure without preoperative urodynamic examination: long-term outcome. Int J Urol 2012 Nov;19(11):1003-9; Serati M, Tension-free Vaginal Tape for the Treatment of Urodynamic Stress Incontinence: Efficacy and Adverse Effects at 10-Year Follow-Up. Eur Urol 2012;61:939-946; Svenningsen R, et al., Long-term follow-up of the retropubic tension-free vaginal tape procedure. Int Urogynecol J 2013 Aug;24(8):1271–8; Jonsson Funk M, et al., Sling revision/removal for mesh erosion and urinary retention: long-term risk and predictors. Am J Obstet Gynecol 2013;208:73.e1–7.

[37] Mistrangelo E, et al., Rising use of synthetic mesh in transvaginal pelvic reconstructive surgery: A review of the risk of vaginal erosion. J Minimally Invasive Gynecol 2007(14):564-69.

[38] Mistrangelo E, et al., Rising use of synthetic mesh in transvaginal pelvic reconstructive surgery: A review of the risk of vaginal erosion. J Minimally Invasive Gynecol 2007(14):564-69.

The safety and efficacy of both the TVT and TVT-O have been well-studied. Systematic reviews and meta-analyses—the highest level of scientific evidence—support the safety and efficacy of full-length mid-urethral slings like the TVT-O. In 2015, Ford and colleagues published a Cochrane Review on mid-urethral sling operations for stress urinary incontinence in women. They performed a systematic review of 81 randomized or quasi-randomized controlled trials involving 12,113 women with SUI, USI, or MUI in which both trial arms involved a mid-urethral sling operation. Their analysis showed that, in the short-term subjective cure with trans-obturator mid-urethral sling procedures ranged from 62-98%, and in the long-term from 43-92%. They found that 6.4% of patients receiving a trans-obturator mid-urethral sling experienced groin pain, and that it was of short duration. The overall rate of vaginal mesh erosion/exposure/extrusion was 2.4% in patients receiving trans-obturator mid-urethral slings. The authors also noted: "There is moderate quality evidence that overall reported rates of tape-related complications are low, such as erosion of the tape into the vagina at about 2% for both routes of tape insertion. The reported occurrence of problems with sexual intercourse including pain was low, and leakage of urine during intercourse are improved following insertion of these tapes." The authors concluded:

> Mid-urethral sling operations have been the most extensively researched surgical treatment for stress urinary incontinence (SUI) in women and have a good safety profile. Irrespective of the routes traversed, they are highly effective in the short and medium term, and accruing evidence demonstrates their effectiveness in the long term. This review illustrates their positive impact on improving the quality of life of women with SUI.[39]

In 2014, the Society of Gynecologic Surgeons' Systematic Review Group published a systematic review and meta-analysis of randomized controlled trials with a minimum of 12 months of follow-up. Based on their analysis, they made clinical practice guidelines for the surgical treatment of SUI. They suggested that, for patients considering midurethral slings or the Burch procedure for treatment of SUI, either intervention could be recommended based on objective and subjective cure rates, and that the decision could be based on (1) which adverse events are of greatest concern to the patient, and (2) whether any other concomitant surgeries were planned. They noted that midurethral slings "may result in lower rates of perioperative adverse events such as blood loss, postoperative pain, operating room time, hospital stay, bowel injury, wound infection, and hematomas," but the Burch procedure "may result in lower rates of return to operating room for retention, erosion, overactive bladder symptoms, and groin pain." For women considering either a pubovaginal sling or the TVT midurethral sling, they recommended the TVT midurethral sling for better subjective cure outcomes, and noted that the TVT "may result in lower rates of perioperative outcomes such as operating room time, blood loss, and hospital stay," while pubovaginal slings "may result in lower rates of adverse events such as urinary tract infection and vaginal perforation." For women considering either a retropubic or transobturator sling, they recommended either one based on objective and subjective cure rates, and suggested that the decision should be based on which adverse events are of greatest concern to the patient, with retropubic slings resulting "in lower rates of sling erosion, need to return to operating room for treatment of sling erosion, groin/leg pain, and vaginal perforation," and transobturator midurethral slings resulting "in shorter operative time, fewer bladder/urethral perforations, less perioperative pain, fewer urinary tract infections,

[39] Ford AA, et al., Mid-urethral sling operations for stress urinary incontinence in women. Cochrane Database Syst Rev. 2015 Jul 1;7:CD006375. doi: 10.1002/14651858.CD006375.pub3.

and less overactive bladder symptoms."[40] The data presented in Table 3 of the study shows that trans-obturator full-length mid-urethral slings like the TVT-O compare very favorably to other surgical treatments for SUI.

In 2015, Dr. Giovanni Tommaselli and colleagues published a systematic review and meta-analysis of medium- and long-term outcomes following mid-urethral sling surgeries. Their study looked at studies involving the treatment of 2,432 patients receiving trans-obturator slings, and noted that "[p]ersistent or chronic pain (i.e. pain persisting beyond the peri-operative period or reported at the last follow-up visit) was reported by . . . 30 patients for [trans-obturator mid-urethral slings]." The authors found that both retropubic and trans-obturator mid-urethral slings "are associated with high objective and subjective cure rates in the long- and medium-term." They also noted that the efficacy of mid-urethral slings "is backed by a high safety profile, and by a limited number of complications which were seldom severe."[41]

Several registry studies involving very large patient populations support the safety and efficacy of mid-urethral slings such as the TVT-O for the treatment of SUI. In 2011, Dr. Mohamed Abdel-fattah and colleagues reported on their register linkage study undertaken to examine the lifetime risk of undergoing pelvic floor surgery in a cohort of parous women from the United Kingdom, as well as the rates of re-operation following pelvic floor surgery. Their study data included 34,631 women identified from the Aberdeen Maternity and Neonatal Database and Scottish Morbidity Records database. The authors found that the re-operation rate for urinary incontinence was 3.2% in the mid-urethral sling group, and 10.7% in the abdominal retropubic surgery group.[42]

Dr. Michele Jonsson Funk and colleagues published a study in 2013 that analyzed—using data from a large insurance claims database—188,454 women who underwent a mid-urethral sling procedure between 2001 and 2010, and found that the nine-year cumulative risk of sling revision or removal was 3.7% The nine-year risk of sling removal or revision due to mesh erosion was 2.5%.[43]

Dr. John N. Nguyen and colleagues reported in 2012 on the results of their study of all female members of Kaiser Permanente Southern and Northern California and Hawaii who underwent sling procedures or pelvic organ prolapse procedures with implanted grafts or mesh between September 1, 2008 and May 31, 2010. The study population was 4,142 women. The authors found that reoperation for mesh erosions following sling procedures were performed on 30 of the 3,747—i.e., 0.8%—women. Only 1.3% of the women receiving slings required reoperation for voiding dysfunction or urinary retention.[44]

In 2015, Dr. Cecile Unger and colleagues published a case-control study of all women undergoing mid-urethral sling placement for SUI at a tertiary care referral center over a ten-year period,

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[40] Schimpf MO, et al., Sling surgery for stress urinary incontinence in women: a systematic review and metaanalysis. Am J Obstet Gynecol 2014;210:1.e1-1.e27.
[41] Tommaselli GA, Medium-term and long-term outcomes following placement of midurethral slings for stress urinary incontinence: a systematic review and metaanalysis. Int Urogynecol J 2015 Sep;26(9):1253-68.
[42] Abdel-fattah M, et al., Primary and repeat surgical treatment for female pelvic organ prolapse and incontinence in parous women in the UK: a register linkage study. BMJ Open 2011;1:e000206. Doi:10.1136/bmjopen-2011-000206.
[43] Jonsson Funk M, et al., Sling revision/removal for mesh erosion and urinary retention: long-term risk and predictors. Am J Obstet Gynecol 2013;208:73.e1–7.
[44] Nguyen JN, et al., Perioperative Complications and Reoperations After Incontinence and Prolapse surgeries Using Prosthetic Implants. Am J Obstet Gynecol 2012 Mar;119(3):539–46.

which amounted to 3,307 patients. Out of those 3,307 women, only 89 (2.7%) required sling revision. Of those 89 women requiring revision, 43.8% (39) had their slings revised for urinary retention, 42.7% (38) for voiding dysfunction, 20.2% (18) for recurrent urinary tract infections, 21.3% (19) for mesh erosion, 7.9% (7) for vaginal pain/dyspareunia, and 3.4% (3) for groin pain. Trans-obturator in-to-out slings like the TVT-O accounted for only 9% of the revisions.[45]

Also in 2015, Welk and colleagues published a population-based retrospective cohort study that included all adult women undergoing SUI surgery with synthetic mesh in Ontario, Canada from April 1, 2002 through December 31, 2012, which amounted to 59,887 women. The authors used three linked databases to compile the study data. The authors found that complications were treated in 1,307 women (2.2%), and that the ten-year cumulative incidence of secondary surgery to treat complications was 3.29%. They noted that ten years after SUI mesh surgery, one out of every thirty women receiving a mesh sling would need a second surgery to remove or revise the mesh.[46]

Numerous organizations have also addressed the safety and efficacy of synthetic mesh midurethral slings.[47] For instance, the American Urogynecologic Society (AUGS) and the Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction (SUFU) issued a position statement in 2014 that noted: "The polypropylene mesh midurethral sling is the recognized worldwide standard of care for the surgical treatment of stress urinary incontinence. The procedure is safe, effective, and has improved the quality of life for millions of women." They also noted: "Full-length midurethral slings, both retropubic and transobturator, have been extensively studied, are safe and effective relative to other treatment options and remain the leading treatment option and current gold standard for stress incontinence surgery. Over 3 million MUS have been placed worldwide and a recent survey indicates that these procedures are used by > 99% of AUGS members.[48]

Gynecologists, Urologists, and Urogynecologists in training learn the use of and the importance of mid-urethral slings for the treatment of SUI. The International Urogynecological Association's guidelines for training in female pelvic surgery state that trainees "must be fully conversant with the indications for, techniques of and complications surrounding," among other things, "minimally invasive

[45] Unger CA, et al., Indications and risk factors for midurethral sling revision. Int Urogynecol J 2016 Jan;27(1):117–22.
[46] Welk B, et al., Removal or Revision of Vaginal Mesh Used for the Treatment of Stress Urinary Incontinence. JAMA Surg. 2015 Dec;150(12):1167-75.
[47] ACOG/AUGS Practice Bulletin No. 155; Nov. 2015; AUGS-SUFU, Position Statement on Mesh Midurethral Slings for Stress Urinary Incontinence (Jan. 3, 2014); AUGS Position Statement on Restriction of Surgical Options for Pelvic Floor Disorders (2013); AUA Position Statement on the Use of Vaginal Mesh for the Surgical Treatment of Stress Urinary Incontinence (Nov. 2011); ICS Fact Sheets: A Background to Urinary and Faecal Incontinence (July 2013); IUGA—Stress Urinary Incontinence—A Guide for Women (2011); FDA, Considerations about Surgical Mesh for SUI (2013); NICE clinical guideline 171. Urinary Incontinence: The management of urinary incontinence in women (Sept. 2013); Lucas, MG, et al., EAU Guidelines on Surgical Treatment of Urinary Incontinence. European Urol 62 (2012) 1118-1129; FDA Executive Summary, Surgical Mesh for Treatment of Women with Pelvic Organ Prolapse and Stress Urinary Incontinence (Sept. 8-9, 2011); AUA Position Statement on the Use of Vaginal Mesh for the Surgical Treatment of Stress Urinary Incontinence (2012); FDA 24-hr Summary—Ob/Gyn Devices Panel (Sept. 8-9, 2011); Dmochowski RR, et al., Update of AUA Guideline on the Surgical Management of Female Stress Urinary Incontinence. J. Urol. 183: 1906-1914 (May 2010).
[48] AUGS-SUFU, Position Statement on Mesh Midurethral Slings for Stress Urinary Incontinence (Jan. 3, 2014)

slings," and both retropubic and trans-obturator sling procedures.[49] And the American Board of Obstetrics and Gynecology and the American Board of Urology Guide to Learning in Female Pelvic Medicine and Reconstructive Surgery indicates that FPMRS fellows should "[p]erform a variety of evidence-based surgical procedures for stress incontinence," "[p]erform and describe the indications, intra and postoperative complications, and success of," among others, retropubic and trans-obturator synthetic sling procedures to treat incontinence.[50] Likewise, the Accreditation Council for Graduate Medical Education (ACGME) Program Requirements for Graduate Medical Education in Female Pelvic Medicine and Reconstructive Surgery states: "Fellows must be able to competently perform all medical, diagnostic, and surgical procedures considered essential for the area of practice. Fellows must demonstrate competence in: … performing surgery for urinary incontinence including native tissue and synthetic slings…."[51] The American Urogynecologic Society (AUGS) Resident Learning Objectives notes that residents must "[u]nderstand the difference between a pubovaginal and mid-urethral sling," and "[u]nderstand and perform a mid-urethral sling using either a retropubic or trans-obturator approach."[52] The American Urological Association's National Medical Student Curriculum on Urinary Incontinence states: "Synthetic mid urethral slings are ideal for the patient with anatomic stress incontinence who is looking for a surgery with minimal recovery time."[53]

The TVT-O is superior to, and an improvement over, alternative procedures such as the Burch Colposuspension and autologous fascial slings. As a result, treatment of SUI with mid-urethral slings has become more common than treatment with Burch procedures or pubovaginal sling procedures.[54]

Based on the peer-reviewed published literature and on my experience, education, and training, it is my opinion that the TVT-O is an excellent and highly useful product. It is a device that can be used in old and young patients, it can be used to treat both stress urinary incontinence and mixed urinary incontinence, and it can be used in both primary surgical cases or cases of recurrent SUI following a prior incontinence surgery. It involves very small incisions rather than the larger incisions necessary for an autologous fascial sling surgery or an open Burch procedure. It avoids the necessity of having a second operative site to harvest autologous graft material as is necessary with the autologous fascial sling procedure.[55] The TVT-O procedure involves a short operative time, short recovery time, and is a simple and straightforward procedure that can be readily learned by a wide variety of surgeons, which, in turn, increases patients' access to surgical treatment for their incontinence. Unlike non-implant-based procedures, the device comes with an Instructions for Use ("IFU") document (discussed below), that provides instructions for using the device, indications, contraindications, warnings, and possible adverse reactions. Both the published literature as a whole and my experience using the TVT-O shows that the

[49] Drutz HP and IUGA Education Committee, IUGA guidelines for training in female pelvic medicine and reconstructive surgery (FPM-RPS), Updated Guidelines 2010, App'x 3.3.
[50] ABOG & ABU Guide to Learning in Female Pelvic Medicine and Reconstructive Surgery 2012.
[51] ACGME Program Requirements for Graduate Medical Education in Female Pelvic Medicine and Reconstructive Surgery
[52] AUGS Resident Learning Objectives
[53] AUA National Medical Student Curriculum on Urinary Incontinence (updated August 2012).
[54] Wood LN and Anger JT, Urinary incontinence in women, BMJ:2014;349:g4531; Schimpf MO, et al., Sling surgery for stress urinary incontinence in women: a systematic review and metaanalysis. Am J Obstet Gynecol 2014;210:1.e1-1.e27; Welk B, et al., Removal or Revision of Vaginal Mesh Used for the Treatment of Stress Urinary Incontinence. JAMA Surg. 2015 Dec;150(12):1167-75.
[55] Mistrangelo E, et al., Rising use of synthetic mesh in transvaginal pelvic reconstructive surgery: A review of the risk of vaginal erosion. J Minimally Invasive Gynecol 2007(14):564-69.

device improves the quality of life of women suffering from SUI. The TVT-O is neither defective nor unreasonably dangerous.

Plaintiffs' experts have suggested that other materials such as Vypro mesh, Ultrapro mesh, or a mesh made from PVDF would have been safer than the Prolene mesh used in the TVT-O, but the published literature does not support such contentions. I am unaware of any studies demonstrating the safety or efficacy of a mid-urethral sling made of PVDF for the treatment of SUI. One study by a group of surgeons in Turkey looked at using Vypro, Ultrapro, or Prolene Soft meshes—each of which have a larger pore size and lighter weight than the TVT-O mesh—in an incontinence surgery, but that study showed that vaginal erosions suture granulomas, urine retention, incontinence, and de novo urgency still occurred in each of the three groups studied. The procedure performed in the study was not similar to the TVT-O procedure, and does not demonstrate the feasibility of using any of these meshes in the TVT-O device. Furthermore, I am unaware of any of these meshes being cleared or approved by the FDA for use in treating stress urinary incontinence.

Ethicon looked into making the TVT-O with a partially absorbable mesh, but encountered a problem with the mesh sticking to the sheaths.[56] Studies involving the use of Ultrapro mesh in the treatment of pelvic organ prolapse indicate that erosions, dyspareunia, and chronic pelvic pain can occur even after the use of that mesh.[57] Vypro mesh has been found to be poorly tolerated in pelvic floor surgery, with high rates of erosion and problems of cicatrisation.[58]

e. Plaintiffs' Theories Are Not Supported by the Published Medical Literature or My Experience.

The systematic reviews, meta-analyses, long-term studies, registry studies, and randomized controlled trials regarding mid-urethral slings—many of which are discussed above—do not show clinically-significant degradation of Prolene mesh. Nor have I seen any evidence of Prolene mesh degradation in my clinical practice—I have not observed degradation of the mesh in the instances in which I have explanted it. I have not found possible degradation to be the cause of complications in any of my patients, nor have I seen any clinical studies showing an increase in complications resulting from any degradation. The excellent safety and efficacy reported in the medical literature discussed above, even out to seventeen years after the procedure, is inconsistent with the idea that the mesh is degrading in vivo. While articles such as the Clavé article may purport to show degradation, the article involved chemical analysis of less than 1/3 of the overall cohort of 100 explants, and even then, only showed degradation in 1/3 of the explants examined with a scanning electron microscope.[59] The Costello article relied on by plaintiffs' experts is a low-level case report. And to reiterate, even if these articles reliably

[56] ETH.MESH.09922570–8, R&D Memorandum on PA Mesh Assessments for TVTO-PA.
[57] Quemener J, et al., Rate of re-interventions after transvaginal pelvic organ prolapse repair using partially absorbable mesh: 20 months median follow-up outcomes. Eur J Obstet Gynecol Reprod Biol 2014;175:194–8; Milani AL, et al., Medium-term clinical outcomes following trocar-guided mesh repair of vaginal prolapse using partially absorbable mesh. Int Urogynecol J 2012;23(Suppl2):S43-S244.
[58] Denis S, et al., Pelvic Organ Prolapse Treatment by the Vaginal Route Using a Vypro® Composite Mesh: Preliminary Results About 106 Cases. 2004 ICS IUGA Abs. #620.
[59] Clavé A, et al., Polypropylene as a reinforcement in pelvic surgery is not inert: comparative analysis of 100 explants. Int Urogynecol J 2010;21:261–70.

confirmed degradation, which in my opinion they do not, I have not found such degradation to be of any clinical significance.

I also have not seen roping, curling, or fraying of the TVT-O mesh. In my experience, if the product is properly handled and implanted per the IFU and professional education training, this does not occur. Nor have I seen fraying or particle loss with the TVT-O mesh. If, however, some particle loss did occur, one would not expect that to be clinically significant, as the particles lost would be the same Prolene suture material that is safely implanted in patients around the world on a daily basis.

Nor have I seen contraction of Prolene mesh in the TVT-O. Scar tissue may contract, but not the mesh itself. Scar formation occurs in connection with the healing process following any surgery, and a certain amount of scarring is necessary and desired in connection with implantation of the TVT-O device. The mesh serves as a scaffold into which scar tissue is incorporated, and it is the mesh and scar tissue that provides the mid-urethral support that makes restores the patient's continence.

There is no credible evidence in the peer-reviewed, published literature indicating that the Prolene mesh used in the TVT-O is carcinogenic. On the contrary, recent literature indicates the mesh is not carcinogenic.[60] Dr. Bradley Linder and colleagues at the Mayo Clinic reported this year that they found "in a large series of patients undergoing synthetic midurethral sling placement with long-term follow-up, no evidence of an association between mesh placement with subsequent local cancer formation."[61]

Neither the published medical literature nor my experience using both types of mesh indicates that there is a clinically significant difference between laser-cut mesh and mechanically cut mesh. I have used both products in my practice over the past ten years, and have not observed a difference in the way the mesh performs based on the way it was cut. Nor does the peer-reviewed published literature discuss a clinically significant difference between the two. Literature prior to 2006—when only mechanically cut mesh was available—and literature after 2006—when both laser-cut and mechanically cut mesh was available—shows the same excellent efficacy and safety overall.

Plaintiffs' experts contend that the Prolene mesh is cytotoxic or creates an excessive foreign body reaction and inflammatory response. Again, this is not consistent with the medical literature on the device or my experience using the device. While some foreign body reaction is to be expected after the implantation of any surgical mesh, that reaction is not excessive. If it were excessive, one would expect persistent or chronic pain associated with the device to be the rule, not the very uncommon exception to the rule.[62] Likewise, if the Prolene in the mesh was actually cytotoxic, one would expect erosions to be

[60] Linder BJ, et al., Evaluation of the local carcinogenic potential of mesh used in the treatment of female stress urinary incontinence. Int Urogynecol J 2016 Feb 10; DOI 10.1007/s00192-016-2961-4; King AB and Goldman HB, Current Controversies Regarding Oncologic Risk Associated with Polypropylene Midurethral Slings. Curr Urol Rep 2014;15:453; Moalli P , et al., Polypropylene mesh: evidence for lack of carcinogenicity. Int Urogynecol J 2014 May;25(5):573-6.

[61] [61]Linder BJ, et al., Evaluation of the local carcinogenic potential of mesh used in the treatment of female stress urinary incontinence. Int Urogynecol J 2016 Feb 10; DOI 10.1007/s00192-016-2961-4.

[62] Tommaselli GA, Medium-term and long-term outcomes following placement of midurethral slings for stress urinary incontinence: a systematic review and metaanalysis. Int Urogynecol J 2015 Sep;26(9):1253-68.

the rule rather than the very uncommon exception to the rule, occurring only approximately 2% of the time.[63]

Plaintiffs' experts also contend that the mesh in the TVT-O device shrinks or contracts. During the tissue incorporation process following implantation of the sling, the tissue that is incorporated can shrink, but that does not create any retention problem if the device is implanted in a tension-free manner as directed by the instructions for use. Based on my review of the medical literature and my experience using the devices, it is my opinion that the mesh itself in the TVT-O device does not shrink, and the tissue incorporated into the device does not excessively shrink or contract. This is evidenced by the long-term studies of the TVT and TVT-O devices discussed above. If excessive contracture/shrinkage was occurring, you would expect to see pain and/or retention problems in the majority of patients, which one does not see.[64]

VI. Ethicon's TVT-O IFU and Other Educational Materials

a. The TVT-O IFUs

Each TVT-O device is accompanied by an Instructions for Use ("IFU") document that describes the device, explains in detail how to implant the device, sets forth contraindications to using the device, warnings and precautions, and potential adverse reactions.[65] The IFU begins with an instruction to the user to "[p]lease read all information carefully," and cautions that "[f]ailure to follow instructions may result in improper functioning of the device and may lead to injury."

While the IFU does instruct surgeons on how to implant the device, it also advises that the "device should be used only by physicians trained in the surgical treatment of stress urinary incontinence and specifically in implanting the GYNECARE TVT Obturator device." The IFU also notes that it "is not a comprehensive reference to surgical technique for correcting SUI (Stress Urinary Incontinence)."

The Warnings and Precautions section of the IFU notes that "[a]cceptable surgical practice should be followed for the GYNECARE TVT Obturator procedure as well as for the management of contaminated or infected wounds." It also advises that the procedure "should be performed with care to avoid large vessels, nerves, bladder and bowel. Attention to patient anatomy and correct passage of the device will minimize risks." The IFU also warns of possible bleeding, transient leg pain, and de novo detrusor instability.

The Adverse Reactions section of the IFU notes that "[p]unctures or lacerations of vessels, nerves, bladder, urethra or bowel may occur during needle passage and may require surgical repair," that

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[63] Schimpf MO, Sling surgery for stress urinary incontinence in women: a systematic review and metaanalysis. Am J Obstet Gynecol 2014;211:71.e1-27; Ford AA, et al., Mid-urethral sling operations for stress urinary incontinence in women. Cochrane Database Syst Rev. 2015 Jul 1;7:CD006375. doi: 10.1002/14651858.CD006375.pub3; Tommaselli GA, Medium-term and long-term outcomes following placement of midurethral slings for stress urinary incontinence: a systematic review and metaanalysis. Int Urogynecol J 2015 Sep;26(9):1253-68.

[64] Athanasiou S, et al., Seven years of objective and subjective outcomes of transobturator (TVT-O) vaginal tape: Why do tapes fail? Int Urogynecol J. 2014;25:219–25; Nilsson CG, et al., Seventeen years follow-up of the tension-free vaginal tape procedure for female stress urinary incontinence. Int Urogynecol J 2013 Aug; 24(8):1265-9; Ford AA, Rogerson L, Cody JD, Ogah J. Mid-urethral sling operations for stress urinary incontinence in women. Cochrane Database of Systematic Reviews 2015, Issue &. Art. No.: CD006375.

[65] ETH.MESH.02340974-80; ETH.MESH.00860239-45.

"[t]ransitory local irritation at the wound site and a transitory foreign body response may occur," which "could result in extrusion, erosion, fistula formation or inflammation." It advises that the mesh may potentiate an existing infection, and that over-tensioning of the device "May cause temporary or permanent lower urinary tract obstruction." Although pelvic floor surgeons are aware that any incontinence surgery could cause temporary or chronic pain or dyspareunia that could be mild, moderate, or severe, the warnings, precautions, and adverse reactions section of the IFU make it clear to surgeons that temporary or chronic pain or dyspareunia could result.

Based on my experience using the TVT-O, my review of the medical literature and other documents I have been provided, it is my opinion that the labeling for the TVT-O device was appropriate for physicians to use the device safely for it intended purposes. The warnings, precautions, and adverse reactions set forth in the IFU are consistent with those reported in the medical literature concerning the device, and with my own experience treating patients with the TVT-O. Warnings regarding carcinogenicity, degradation, contracture/shrinkage, and cytotoxicity would be contrary to the high-level clinical literature regarding TVT-O use and therefore should not, in my opinion, have been included in the IFU.

In evaluating product warnings for a surgical device, one must bear in mind the knowledge base that any pelvic floor surgeon would already possess before reading the IFU. It is commonly known among pelvic floor surgeons that all incontinence surgeries carry a potential risk of hematoma, bladder or bowel injury, lower urinary tract infection, vascular injury, infection, urinary retention, persistent SUI, bleeding, pain, dyspareunia, fistula, de novo urge incontinence, and worsening urge incontinence.[66] It is also commonly known by pelvic floor surgeons that any of these complications, if they occur, could be temporary or permanent, and they could be mild, moderate, or severe. In my opinion, surgeons do not need to be explicitly warned in the IFU of all of these issues.[67] In 2015, Ethicon updated the adverse reactions section of the TVT-O IFU to include some of these risks.[68] In my opinion, it was not necessary, as the risks are commonly known to experienced pelvic floor surgeons.

[66] Ward K and Hilton P, Prospective multicenter randomised trial of tension-free vaginal tape and colposuspension as primary treatment for stress incontinence. BMJ 2002 Jul 13;325(7355):67; Schimpf MO, et al., Sling surgery for stress urinary incontinence in women: a systematic review and metaanalysis. Am J Obstet Gynecol 2014;210:1.e1-1.e27; FDA Considerations about Surgical Mesh for SUI ("The use of mesh slings in transvaginal SUI repair introduces a risk not present in traditional non-mesh surgery for SUI repair, which is mesh erosion, also known as extrusion."); ACGME Program Requirements for Graduate Medical Education in Female Pelvic Medicine and Reconstructive Surgery ("Completing the F3 year must demonstrate competence in their knowledge of … indications, contraindications, limitations, complications, techniques … for … urinary incontinence."); AUGS Resident Learning Objectives (noting that residents must "[u]nderstand the benefits, risks, and how to decide on a vaginal versus abdominal versus combined surgical procedures for the correction of urodynamic stress incontinence"); ABOG & ABU Guide to Learning in Female Pelvic Medicine and Reconstructive Surgery 2012 (noting that FPMRS fellows should describe the intra- and post-operative complications of sling and non-sling incontinence surgeries, and to identify, evaluate, and manage complications associated with incontinence surgery such as foreign body associated complications).

[67] 21 CFR 801.109(c); FDA Device Labeling Guidance #G91-1 (Mar 8, 1991); HMESH_ETH_11642462–81, § 6.1.2.

[68] TVT-O 2015 IFU.

b. Ethicon's Training Programs

In addition to reviewing the IFU, I learned about the TVT-O device when I attended a one-day course regarding the device. It consisted of several hours of didactic lecture, followed by a cadaver lab, during which I had the opportunity to implant a device in a cadaver. I had ample time to ask questions about the device and procedure during the training, and complications were discussed. I found the training to be very helpful, and the supplied course materials were extremely helpful for later review.

c. Ethicon's Product Brochures

I have reviewed the brochures for the TVT-O and find them to be an accurate and helpful tool for surgeons to communicate with their patients regarding the TVT-O device, its benefits, its risks, stress urinary incontinence in general, and alternative treatment options. The brochures explain the various types of incontinence, discuss how SUI occurs, how it is diagnosed, provide possible questions the patient may want to ask the surgeon, they describe alternative non-surgical treatment options, and explain how the device works and how it may be able to help the patient. The brochures discuss risks such as difficulty urinating, injury to blood vessels of the pelvic sidewall and abdominal wall, bladder injury, bowel injury, punctures or lacerations requiring surgical repair, extrusion, erosion, fistula formation, inflammation, infection, and urinary tract obstruction.[69] Some of the brochures also warned of pain, scarring, pain with intercourse, and mesh exposure, and explained that synthetic mesh is a permanent medical device implant.[70] The brochures discuss these matters in terms that patients can understand. I have used and continue to use the brochures in my practice and, while they are not a substitute for a full discussion with the patient about the procedure and device, they constituted one aspect of the discussion I have with patients regarding the device.

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[69] E.g., ETH.MESH.00658421-9; ETH.MESH.01613143-6; ETH.MESH.08003181-96; ETH.MESH.08003197-212; ETH.MESH.08003231-46; ETH.MESH.03458123-38; ETH.MESH.08003215-30; ETH.MESH.08003247-62; ETH.MESH.08003263-78.

[70] ETH.MESH.08003279-94.